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[Title of the Invention] Patch for Treating Dermatitis

[Abstract]

[Object]

To provide a patch for treating dermatitis, atopic dermatitis and dermal pruritus being alleviated only by applying the patch to the affected skin areas with these dermatitides.

[Means for Solving the Problems]

An adhesive layer for applying a patch to the skin is formed directly or via an undercoat on one surface of a substrate film, such as polyurethane, which has a thickness of 10 to 80 μm and exhibits moisture permeability. The moisture permeability of the entire portion of the patch is adjusted to be within the range of from 300 to 1500 g/m^2. An acrylic adhesive which has an adhesive force of 30 to 180 g/25 mm width and is obtained by copolymerizing a (meth)acrylic alkyl ester as a main component is preferably used.

[Claims]

1. A patch for treating dermatitis comprising a substrate film which has a thickness of 10 to 80 μm and exhibits moisture permeability having directly or indirectly formed on one surface thereof an adhesive layer for applying the patch to the skin, wherein the moisture permeability of the patch is adjusted to be within the range of from 300 to 1500 g/m^2.

2. The patch for treating dermatitis according to claim 1, wherein the substrate film is at least one polymer type selected from polyether polyurethanes, polyester polyurethanes, polyether-polyamide block polymers.

3. The patch for treating dermatitis according to claim 1, wherein the adhesive force of the adhesive layer for applying the patch to the skin is 30 to 180 g/25 mm.
4. The patch for treating dermatitis according to claim 3, wherein the adhesive layer for applying the patch to the skin is comprised of an acrylic adhesive obtained by copolymerizing a (meth)acrylic alkyl ester as a main component.
[Detailed Description of the Invention]
[0001]
[Technical Field of the Invention]

The present invention relates to a patch for treating dermatitis.

[0002]
[Prior Art]

Recent years, among dermatitides, atopic dermatitis has frequently occurred due to the change in dietary habit, living environment and mental health issues. Atopic dermatitis occurring in infancy is accompanied by bright red macules which are severely exudative, which first appear in the head, the face and the neck and then extend to the four limbs, while these symptoms tend to be gradually alleviated as patients go through childhood and grow to be in a higher-grade at an elementary school. Although the bright red tone of the skin is decreased, atopic dermatitis becomes chronic in many cases where skin dryness and follicular hyperkeratosis are confirmed.

[0003]

As described above, 30 to 40 %, sometimes 50 % or more of young children in their childhood are affected with atopic dermatitis. Many of them get better, while the ratio of young children with uncured atopic dermatitis is actually increased. In addition, recently, the number of adults suffering from chronic atopic dermatitis as well as the number of children suffering from chronic atopic dermatitis is increased. Advanced countries including Japan have the same situation.

[0004]

The most suffering symptom of patients with atopic

dermatitis is pruritus. Pruritus cannot be tolerated, compared with pain, and it paroxysmally occurs. In addition, dermatitides with pruritus, other than atopic dermatitis, include dermal pruritus typified by senile pruritus.
[0005]

Atopic dermatitis is presumed to be caused by food allergy, house dust, mites and the like. Regarding the causes other than food allergy, after inflammation is caused on the skin, the skin surface becomes extremely dry. As a result, the entry of an antigen from the outside into the inside of the skin occurs to cause an allergenic reaction. The linkage and the causative substance each is not presumed to be one, and plural factors are often complexly intertwined to each other. Therefore the linkage and the causative substance cannot be easily explained. The sense of pruritus produced at the site of inflammation is intolerable, and in reality, adults as well as infants and children usually scratch the site. However, the skin wounded by scratching allows an easier entry of an antigen, and the vascular permeability is increased by scratching, whereby immunocompetent cells are infiltrated and the symptom of inflammation becomes aggravated.
[0006]

As a method for treating said atopic dermatitis, applying corticosteroid (a steroid) and oral administration of an antihistamine are generally performed for inhibiting inflammation at the site of inflammation. However, the steroid has drawbacks that it is strongly effective but its side effects are also strong, and if inflammation occurs over extensive areas, applying a steroid to the whole areas is difficult. Further, if the administration of a steroid is stopped when a temporary remission due to the steroid is observed, the atopic dermatitis relapses, i.e., so-called the rebound phenomenon.
[0007]

On the other hand, in order to improve the environment inside the house, a method for completely removing mites, dead mites, and dirt in the house (cotton dust, house dust and the

like), and a method for completely removing indigenous bacteria on the skin (for example, Staphylococcus aureus and the like) could be performed, but it is not possible to achieve these environments. If it is possible, lots of money would be necessary to achieve these environments.

[0008]

As described above, the actual situation is that there is no method for completely treating atopic dermatitis and curing the same.

[0009]

[Problems to be Solved by the Invention]

The inventors of the present application consider said problems, and keenly studied for treating atopic dermatitis. As a result, they found that remarkably excellent therapeutic effects on atopic dermatitis and dermal pruritus can be obtained by using a topical patch for applying to the skin which exhibits specific moisture permeability, and completed the present invention.

[0010]

[Means for Solving the Problems]

More specifically, the object of the present invention is to provide a patch for treating dermatitis comprising a substrate film which exhibits moisture permeability and has a thickness of 10 to 80 μm having directly or indirectly formed on one surface thereof an adhesive layer for applying the patch to the skin, wherein the moisture permeability of the patch is adjusted to be within the range of from 300 to 1500 g/m^2.

[0011]

Particularly, if the substrate film of the patch is comprised of a polymer type selected from polyether polyurethanes, polyester polyurethanes and polyether-polyamide block polymers, the patch becomes more effective. In addition, more effects can be obtained if the adhesion force of the adhesive layer for applying the patch to the skin is from 30 to 180 g/25 mm. In order to adjust the adhesive force thereof to fall within said range, it is

preferable to use an acrylic adhesive obtained by copolymerizing a (meth)acrylic acid alkyl ester as a main component, as the adhesive layer for applying the patch onto the skin.

[0012]

[Mode for Carrying Out the Invention]

In order to obtain a patch which has flexibility and is not unintentionally removed from the skin during stretching of the skin, a plastic film having the thickness of 10 to 80 μm, more preferably 20 to 50 μm, and exhibiting an appropriate moisture permeability during the application to the skin of a patch comprising the film is used as the substrate film used for the patch for treating dermatitis of the present invention. Urethane polymers such as polyether polyurethanes, polyester polyurethanes and the like, polyether-polyamide block polymers and the like may be used as specific materials of this film. In addition, in order to provide the patch with an appropriate self-supporting property upon application to the skin, a textile such as a non-woven or woven textile may be laminated on one or both surfaces of the support unless the moisture permeability of the support would not be reduced.

[0013]

25 % modulus of said substrate film is preferably adjusted to be 30 kg/cm^2 or less, more preferably within the range of from 5 to 20 kg/cm^2, in order to obtain a film which is not removed from the skin during the stretching of the skin and does not irritate the skin.

[0014]

On the other hand, an adhesive layer for applying the patch to the skin is formed on one surface of said substrate film directly or indirectly via an undercoat for improving anchor effects. In the present invention, it is important that the moisture permeability of a patch with the adhesive layer for applying the patch to the skin is adjusted to be within the range from 300 to 1500 g/m^2. Accordingly, the moisture permeability of the adhesive layer should be adjusted to be within the range

of from 800 to 3000 g/m^2 (when the adhesive layer has a thickness of 30 μm).

[0015]

In addition to the feature that the adhesive layer should have an appropriate skin adhesion property, the adhesive layer should not cause pain and irritation on the skin when removed from the skin, and thus the adhesion force of the adhesive layer is preferably adjusted to be within the range of from 30 to 180 g/25 mm, more preferably 50 to 150 g/25 mm. Note that the adhesive force described in the present invention means the value obtained by applying a patch to the human skin and then conducting a 180-degree peeling test at a tension rate of 300 mm/min using an autograph (SHIMADZU CORPORATION).

[0016]

Said adhesive layer for applying a patch to the skin is preferably comprised of an adhesive which has been conventionally used for medical purposes and does not cause rash upon application to the skin, such as an acrylic adhesive, a natural rubber adhesive, a synthetic rubber adhesive, a silicone adhesive, a vinyl ester adhesive, a vinyl ether adhesive and the like. Among them, considering the features of adhesives, i.e., stability in quality, adhesive characteristics and easy adjustment of moisture permeability, an acrylic adhesive obtained by copolymerizing a (meth)acrylic alkyl ester as a main component is preferable. Specifically, an ester obtained from a primary, secondary or tertiary alcohol having 2 to 18 carbon atoms of the alkyl group, more preferably 4 to 12 carbon atoms thereof and acrylic acid or methacrylic acid may be used as the (meth)acrylic alkyl ester.

[0017]

Specific examples of monomers copolymerizable with said (meth)acrylic acid alkyl ester include monomers which have at least one unsaturated double bond involved in the copolymerization reaction and have a functional group at the side chain, such as a carboxyl group {for example, (meth)acrylic acid, itaconic acid, maleic acid, anhydrous maleic acid and the

like}, a hydroxyl group {such as (meth)acrylic acid hydroxyethyl ester, (meth)acrylic acid hydroxypropyl ester and the like}, sulfoxy group {for example, styrenesulfonic acid, allyl sulfonic acid, (meth)acrylic acid sulfopropyl ester, (meth)acryloyl oxynaphthalenesulfonic acid, acrylamide methylpropanesulfonic acid and the like}, an amino group {for example, (meth)acrylic acid aminoethyl ester, (meth)acrylic acid dimethylaminoethyl ester, (meth)acrylic acid tert-butylaminoethyl ester and the like}, an amide group {for example, (meth)acrylamide, dimethyl(meth)acrylamide, N-butylacrylamide, N-methylol(meth)acrylamide, N-methylolpropane(meth)acrylamide}, and an alkoxyl group {for example, (meth)acrylic acid methoxyethyl ester, (meth)acrylic acid ethoxyethyl ester, (meth)acrylic acid methoxy ethylene glycol ester, (meth)acrylic acid methoxy diethylene glycol ester, (meth)acrylic acid methoxy polyethylene glycol ester, (meth)acrylic acid ethoxy polyethylene glycol ester, (meth)acrylic acid tetrahydrofurfuryl ester and the like}. Examples of other copolymerizable monomers which may be used in the present invention include (meth)acrylonitrile, vinyl acetate, vinyl propionate, N-vinyl-2-pyrrolidone, methylvinylpyrrolidone, vinyl pyridine, vinyl piperidone, vinyl pyrimidine, vinyl piperazine, vinyl pyrazine, vinyl pyrrole, vinyl imidazole, vinyl caprolactam, vinyl oxazole, vinyl morpholine and the like.

[0018]

One or more of these copolymerizable monomers may be copolymerized. However, considering adhesion characteristics, i.e., adhesive properties, the aggregation property and adjustment of moisture permeability, it is preferable to use at least one monomer selected from monomers having a carboxyl group, monomers having an alkoxyl group and monomers having a hydroxyl group as an essential component, and as necessary another monomer from said other monomer examples which is copolymerized with the above monomer.

[0019]

A copolymer obtained by copolymerizing 40 wt% or more of a (meth)acrylic acid alkyl ester, preferably 50 to 98 wt% of one or more types of (meth)acrylic acid alkyl esters with 2 to 50 wt% of one or more types of copolymerizable monomers is used as said acrylic adhesive.

[0020]

As described above, the patch for treating dermatitis of the present invention comprises a substrate film having formed on one surface thereof an adhesive layer for applying the patch to the skin. As necessary, the surface of the adhesive layer is preferably laminated with a separator (release paper) prepared by coating a known release agent on one or both sides of a plastic film or a paper substrate.

[0021]

When the patch of the present invention is used, the separator is just peeled and removed to expose the adhesive layer surface for applying the patch to the affected areas (the skin surface) of patients with atopic dermatitis and dermal pruritus. There is no need to additionally use a steroid and the like. The reasons that atopic dermatitis and dermal pruritus are cured only by applying the patch are not clear, but are presumed as below.

[0022]

Basically, on the skin surface affected with atopic dermatitis and the like, corneocytes on the surface layer of the skin are relatively dry and contracted, compared with healthy skin, whereby the barrier function thereof is reduced. Therefore, the entry of an antigen into the inside of the skin via the area where the barrier function of the skin is reduced easily occurs, inflammation is caused inside of the skin or on the surface thereof, as a result, pruritus is generated and inflammation is further aggravated by scratching. The patch of the present invention is to prevent this malignant circle, has moisture permeability at the same degree as that of the healthy skin, and thus if it is applied to the skin surface, the skin surface will not become dry and the moisture content

of corneocytes in the contracted affected area is increased, whereby corneocytes swell and the barrier function thereof returns.

[0023]

In addition, the entry of an antigen substance from the outside can be prevented by covering the affected areas, wounds and contamination by scratching can be prevented, and thus aggravation of inflammation can be prevented.

[0024]

Note that there is no need for the adhesive layer of the patch of the present invention to contain a steroid exhibiting strong efficacy, but it may contain a medicament such as an anti-inflammatory agent, an antibacterial agents, a bactericide, a cytokine and the like in an amount within the range of from 0.01 to 10 wt% in order to alleviate inflammation in the affected areas.

[0025]

Further, as the patch of the present invention is applied to relatively large skin areas of inflammation, the size of the patch is preferably 5 cm^2 or more, more preferably about 15 to 600 cm^2.

[0026]

[Effects of the Invention]

As described above, the patch for treating dermatitis of the present invention has an effect, which is exhibited only by applying said patch to the affected area with atopic dermatitis and dermal pruritus for several weeks. In addition, the curing efficiency is improved without hurting the affected skin area because the patch is prepared to have appropriate moisture permeability and adhesive force.

[0027]

[Examples]

The present invention will be more specifically explained by showing examples of the present invention below, but the present invention is not limited by the examples and may be variously modified unless the technical idea of the modified

invention is beyond the scope of the present invention. Note that the descriptions "part(s)" in the following text all mean parts by weight.

[0028]

Example 1

An acrylic adhesive (a copolymer of 65 parts of octyl acrylate/35 parts of vinyl acetate) was used and laminated on one surface of a polyether polyurethane (having a thickness of 30 μm) to form an adhesive layer having a thickness of 40 μm. Next, a separator was coated and laminated on the surface of the adhesive layer, and the laminate was cut into the size of 5 cm x 6 cm to prepare a patch of the present invention.

[0029]

Example 2

A patch of the present invention was prepared in the same manner as in the example 1 except that an acrylic adhesive comprised of a copolymer comprising 70 parts of octyl acrylate, 25 parts of ethoxyethyl acrylate and 5 parts of acrylic acid was used as an adhesive.

[0030]

Example 3

A patch of the present invention was prepared in the same manner as in the example 1 except that a polyether-polyamide block polymer (having a thickness of 30 μm) was used as a substrate film, and an acrylic adhesive of the example 2 was used as an adhesive.

[0031]

Example 4

A hydrocolloid adhesive comprising 55 parts of a mixture of carboxymethylcellulose and pectin at a ratio of 2/1 which was uniformly dispersed in 45 parts of a first polyisobutylene (having a weight-average molecular weight of 50,000) and a second polyisobutylene (having a weight-average molecular weight of 1,200,000) at a ratio of 8/2 was used and laminated on one surface of a polyether-polyamide block polymer (having a thickness of 10 μm) having laminated on one surface thereof

with a urethane non-woven textile (having a basis weight of 30 g/m^2) as a substrate film so as to laminate an adhesive layer having a thickness of 40 μm. Next, a separator was coated and laminated on the surface of the adhesive layer, and the laminate was cut into a size of 5 cm x 6 cm to prepare a patch of the present invention.

[0032]

Comparative Example 1

A patch was prepared in the same manner as in the example 2 except that a polyethylene (having a thickness of 30 μm) was used as a substrate film.

[0033]

Comparative Example 2

A patch was prepared in the same manner as in the example 4 except that the hydrocolloid adhesive of the example 4 was replaced with a mixture comprising a first polyisobutylene (having a weight-average molecular weight of 50,000) and a second polyisobutylene (having a weight-average molecular weight of 1,200,000) at a ratio of 8/2.

[0034]

Comparative Example 3

A patch was prepared in the same manner as in the example 2 except that the adhesive layer of the example 2 was coated on one surface of a substrate film so as to have a lattice-shaped pattern and cover 50 % or more of the film surface with the adhesive layer.

[0035]

The patches prepared in said examples and comparative examples were subjected to the following tests. The results thereof are shown in Table 1.

[0036]

<Moisture Permeability>

10 ml of distilled water was poured into a glass vessel having an inner diameter of 8 mm and a height of 40 mm, and the upper opening of the glass vessel was covered in such a manner that an adhesive layer of each patch cut into the size of a

diameter of 50 mm was opposed to the bottom of the vessel. Next, this was put into a temperature-controlled incubator at 40 □C, and 30 % R. H. After it had been left to stand for 24 hours, the reduction in an amount of water was determined to calculate permeated amount of water vapor (g/m^2,day). The value thereof was defined as moisture permeability.

[0037]

<Adhesive Force>

Each patch was cut into a test specimen having a length of 100 mm and a width of 25 mm, was applied to the human back in a longitudinal direction, and then an autograph manufactured by SHIMADZU CORPORATION was used to conduct a peeling test for determining the adhesive force. The value of the adhesive force in terms of an average value of the adhesive force of the specimens where the number of specimen was 3 was obtained using a peeling rate of 300 mm/min.

[0038]

<Allergenic Potency> (Dermal Sensitization)

It was tested in accordance with the Adjuvant and Path Test method. 20 guinea pigs (10 for sensitized group; and 10 for nonsensitized group) were used for the tests using one type of the patches. Additional 20 guinea pigs (10 for sensitized group; and 10 for nonsensitized group) were used for the tests with a positive control substance.

[0039]

The following reagents (1) to (3) were prepared.

(1) An emulsion of Freund Adjuvant

(2) A patch

(3) A positive substance: DNCB (2,4-dinitrochlorobenzene)

[0040]

The hair on the blade bones of 10 guinea pigs in the sensitized group was removed, and the emulsion (1) was intradermally administered. The site of administration was hurt so to give a wound in the shape of #, the patch (2) was applied for 24 hours so as close the wounded site, and this process was continuously repeated three times. Next, after one

week, the site of administration was treated (coated) with sodium lauryl sulfate, and then the patch (2) was applied for 48 hours. Regarding the positive substance (3), positive substance-containing filter paper was used in place of the patch, and the same process as described above was performed.

[0041]

Next, two weeks after said treatment, the hair on the flank of 10 guinea pigs of the sensitized group and 10 guinea pigs of the nonsensitized group was removed, and the patch (1) or the positive substance (3) was applied.

[0042]

24 hours after the application, the patches or the positive substances were removed, and the skin reactions on the application sites were observed 24 hours, 48 hours and 72 hours after the application of the patches and the positive substance.

[0043]

In the determination of the effects of the patches, when there was no difference in the skin reactions between 10 guinea pigs of the sensitized group and 10 guinea pigs of the nonsensitized group, it was concluded that the patch did not have allergenic potency; while when the guinea pigs of the sensitized group exhibited more reaction than those of the nonsensitized group, it was concluded that the patch had allergic potency.

[0044]

<Alleviation of Atopic Dermatitis>

Each patch was applied to the skin surface of a patient with an allergic inflammation symptom, and the degree of alleviation was determined by observing the symptoms one week and three weeks after the application of the patch. Note that the application of the patch was continuously performed for 24 hours/day during said periods of time.

[0045]

[Table 1]

		Moisture permeability (g/m^2, day)	Adhesive force (g/25 mm width)	Allergic potency	Degree of alleviation	
					After one week	After three weeks
Examples	1	950	100	None	Alleviated	Remarkably alleviated
	2	1100	95	None	Alleviated	Remarkably alleviated
	3	1200	95	None	Alleviated	Remarkably alleviated
	4	500	110	None	Relatively alleviated	Alleviated
Comparative examples	1	100	100	None	Aggravated	Aggravated
	2	30	120	None	No change	Relatively aggravated
	3	2500	70	None	No change	Relatively alleviated